

Supplementary Figures

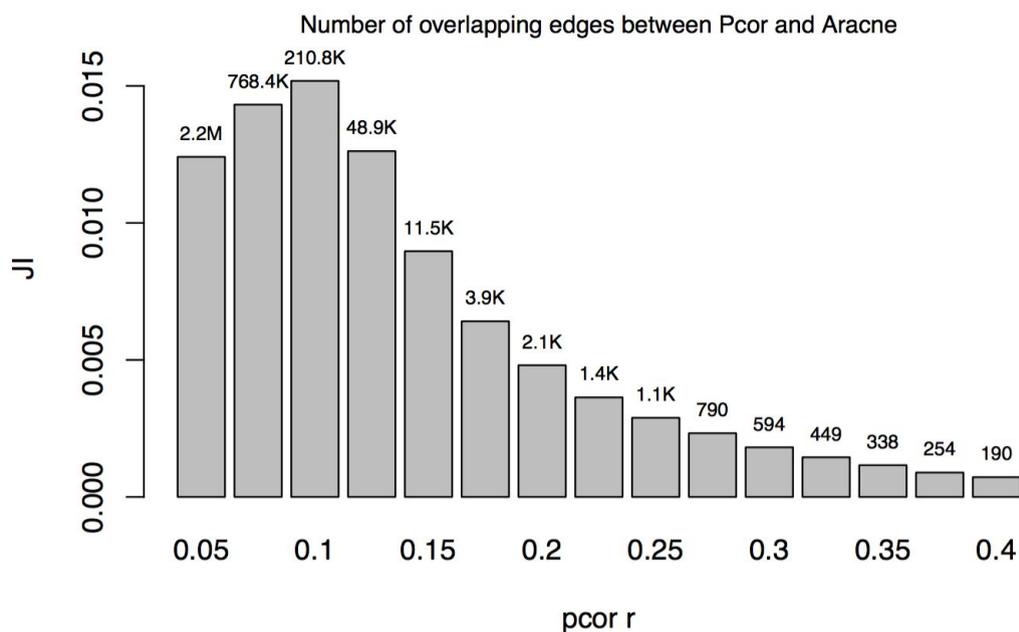


Fig. S1: Sheer number of overlapping edges at different Pcor thresholds.

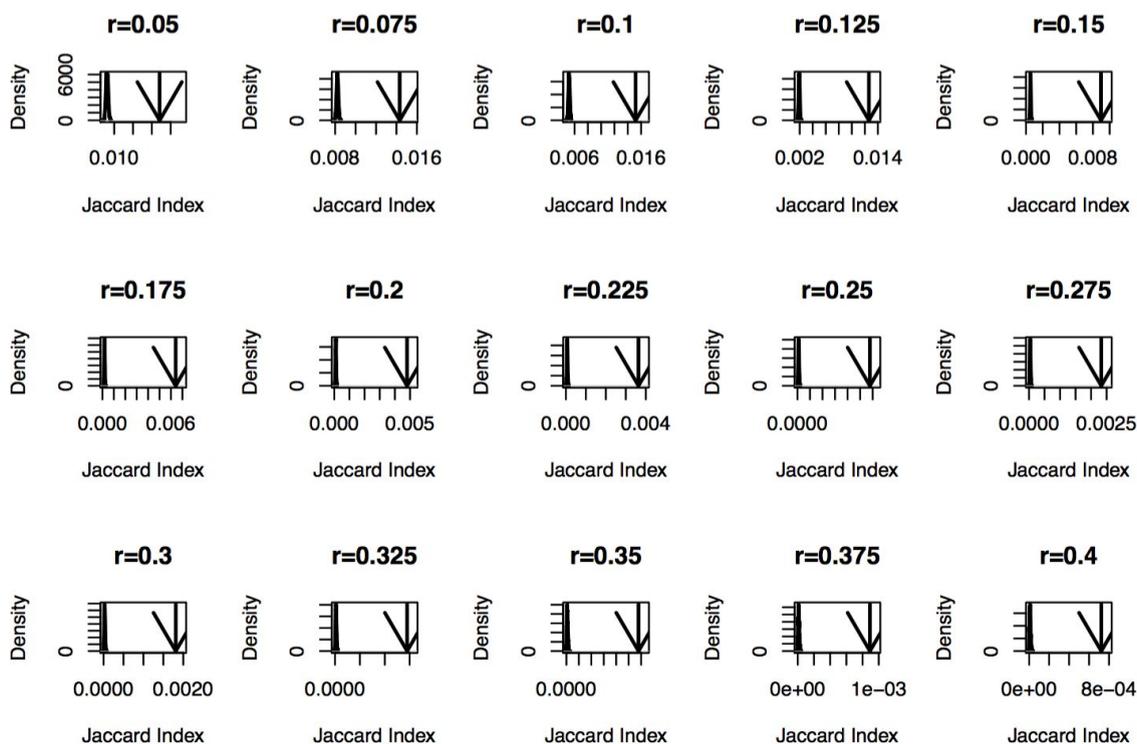


Fig. S2: Comparing the Jaccard Index between the ARACNe network and Partial Correlation networks (indicated as arrows) and Random networks (indicated as distributions).

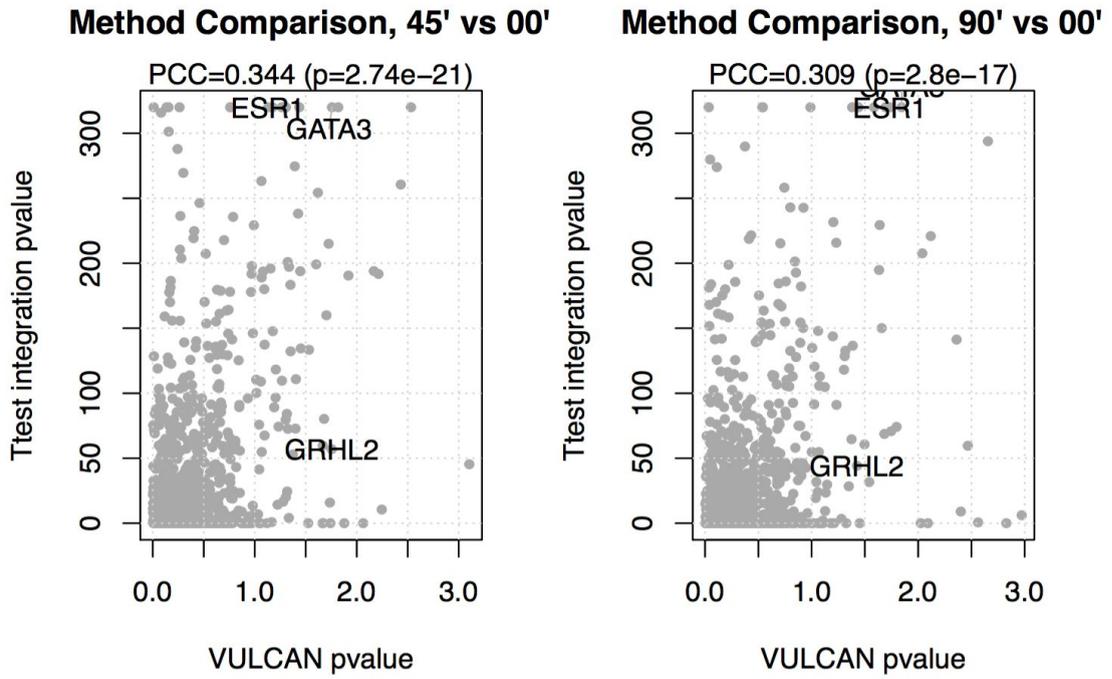


Fig. S3: Comparison between VULCAN/VIPER and T-test integration.

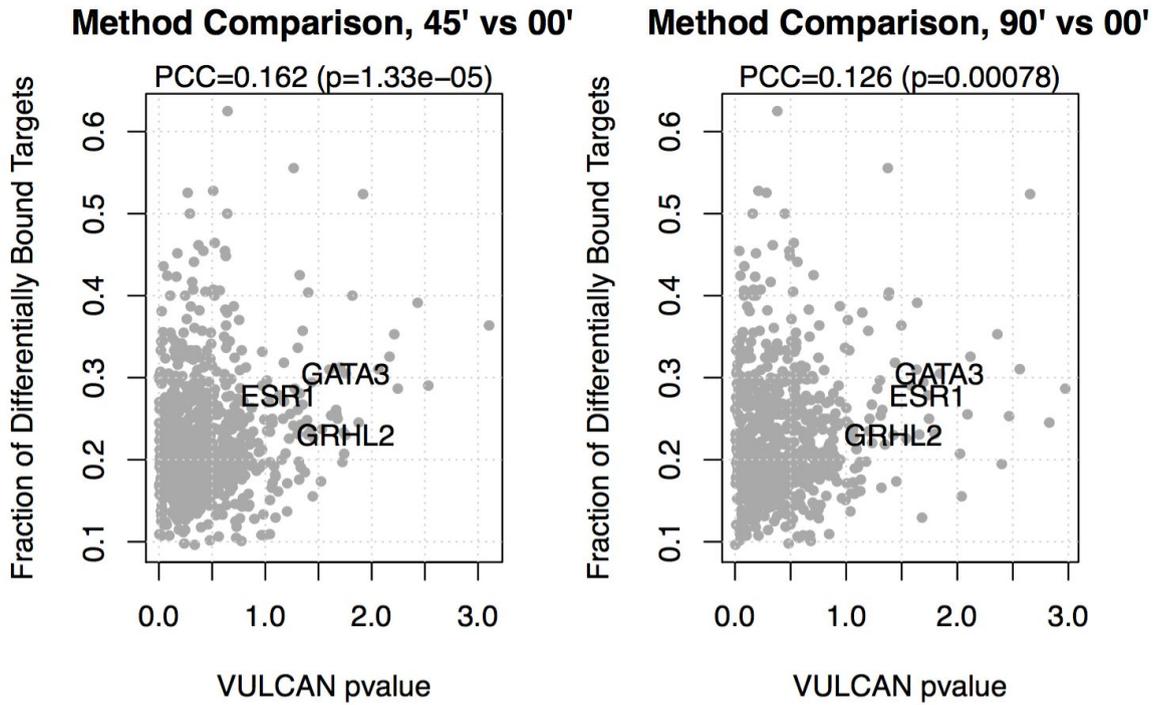
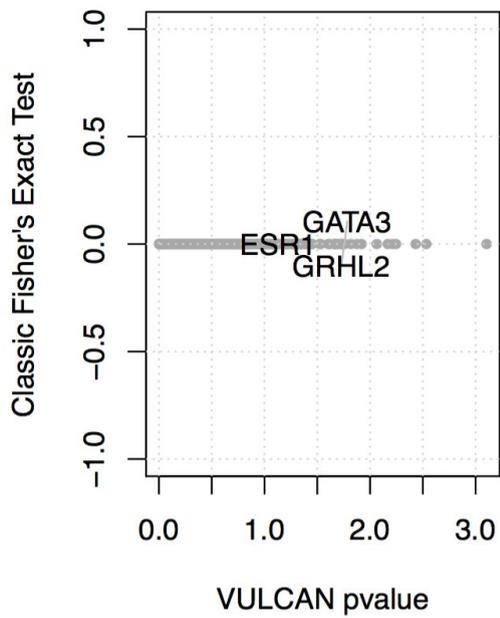


Fig. S4: Comparison between VULCAN/VIPER and a fraction of targets found method.

Method Comparison, 45' vs 00'



Method Comparison, 90' vs 00'

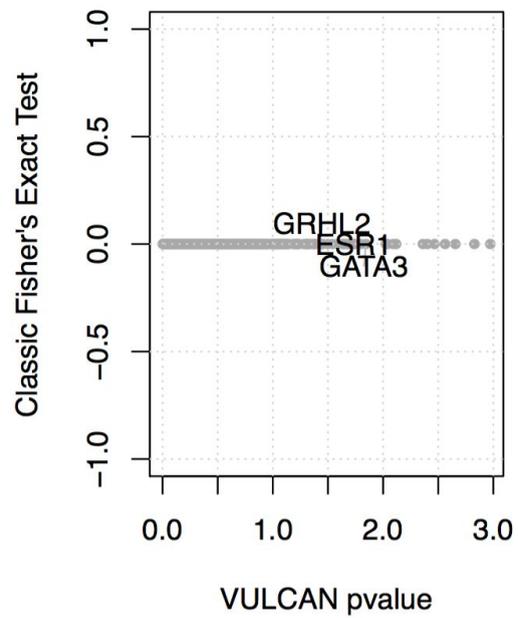
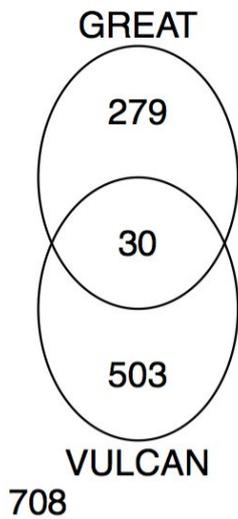


Fig. S5: Comparison between VULCAN/VIPER and Fisher's Exact Test method.

FET p-value: $2.044e-29$



FET p-value: $2.118e-28$

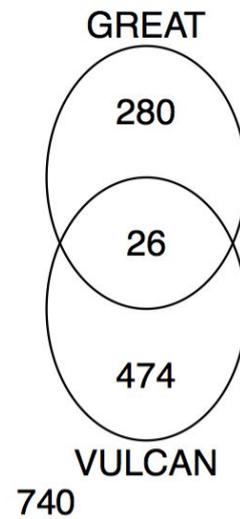


Fig. S6: Comparison of results from the VULCAN and GREAT methods.

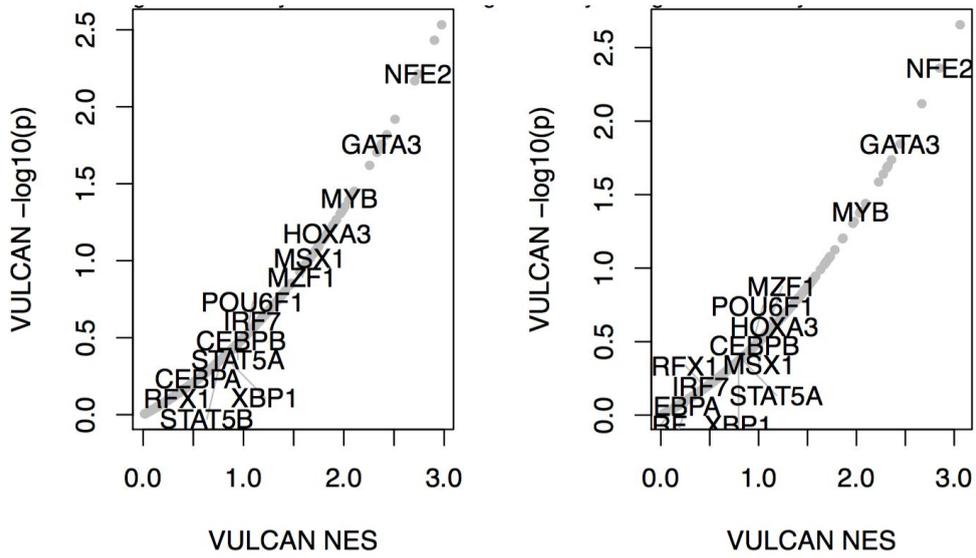


Fig. S7: Comparison of results from the VULCAN and ChIP-enrich methods.

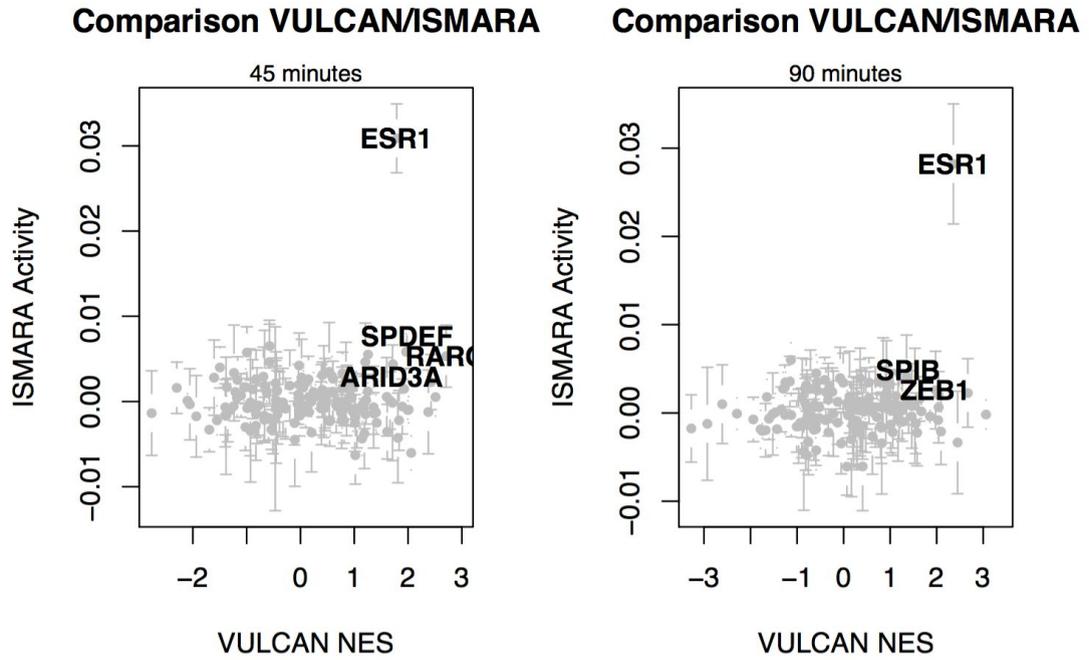


Fig. S8: Comparison of results from the VULCAN and ISMARA methods.

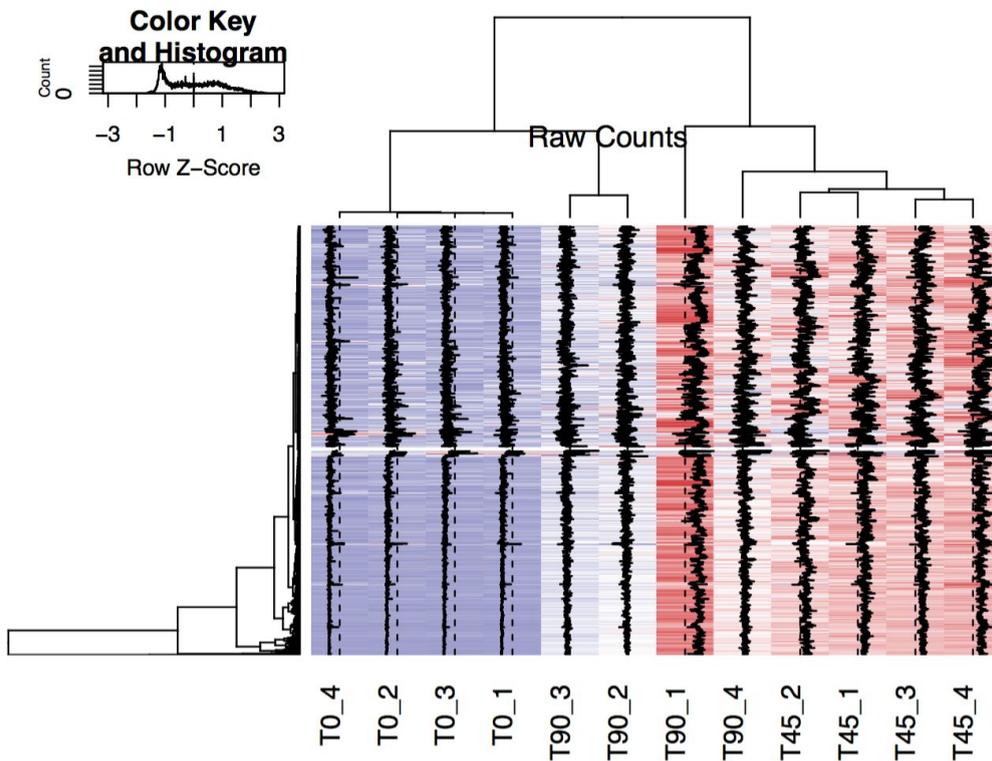


Fig. S9: Dataset clustering with Raw Counts.

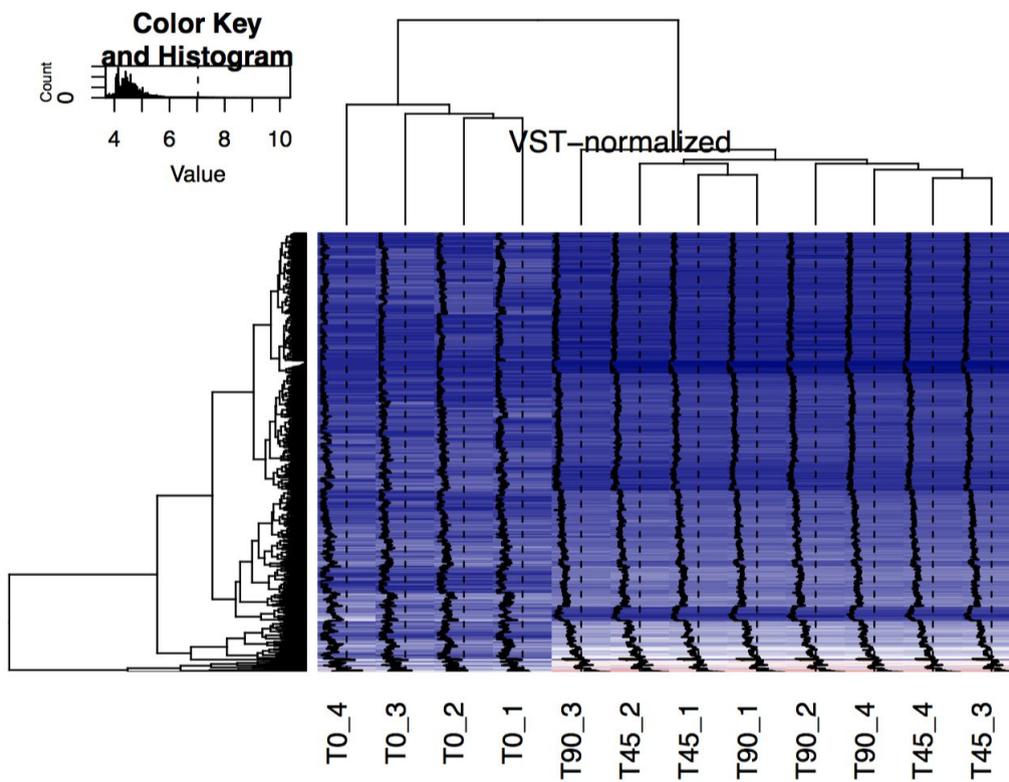


Fig. S10: Dataset clustering with VST-normalized Counts.

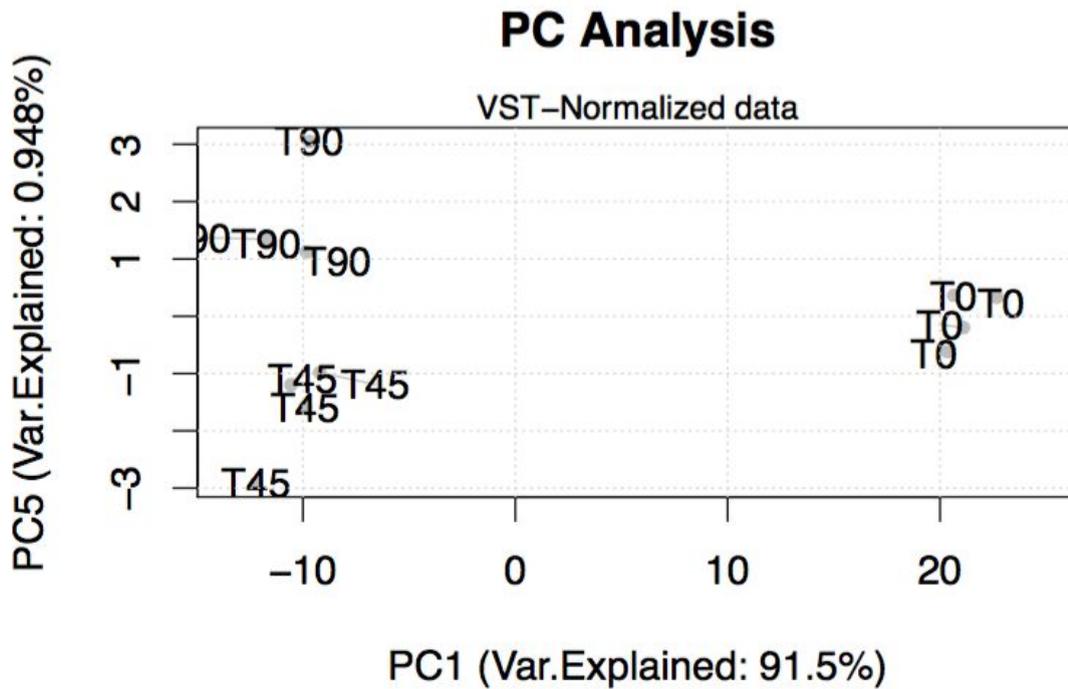


Fig. S13: Principal Component Analysis of the dataset, highlighting components 1 and 5.

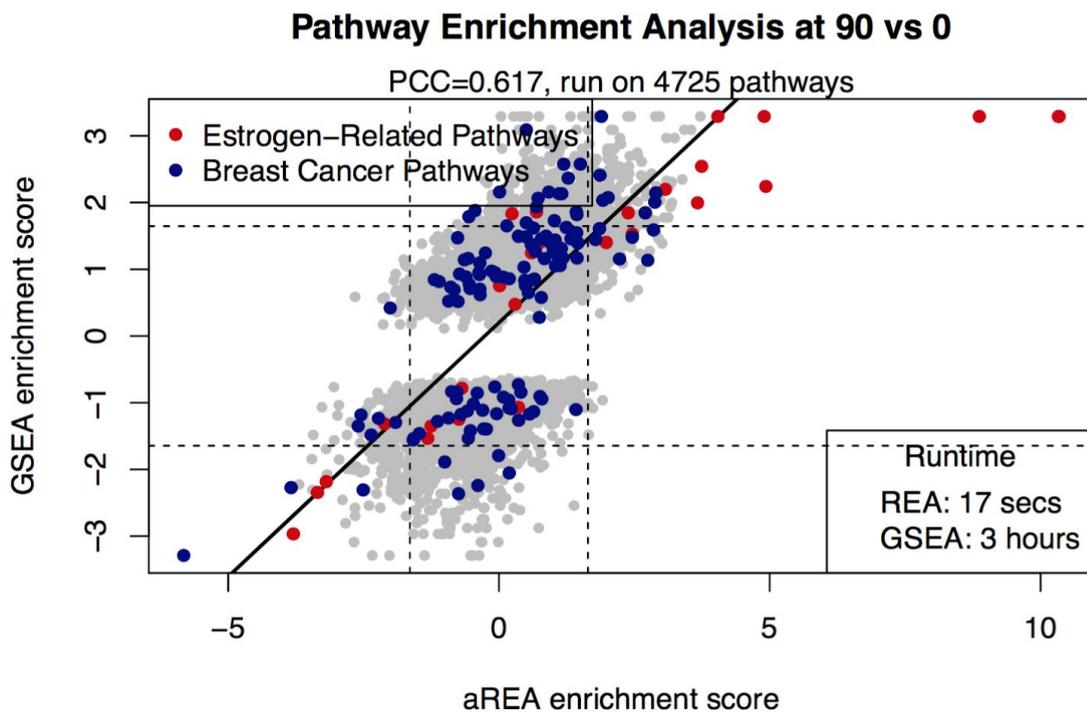


Fig. S14: Comparison of GSEA and aREA on a differential binding signature.

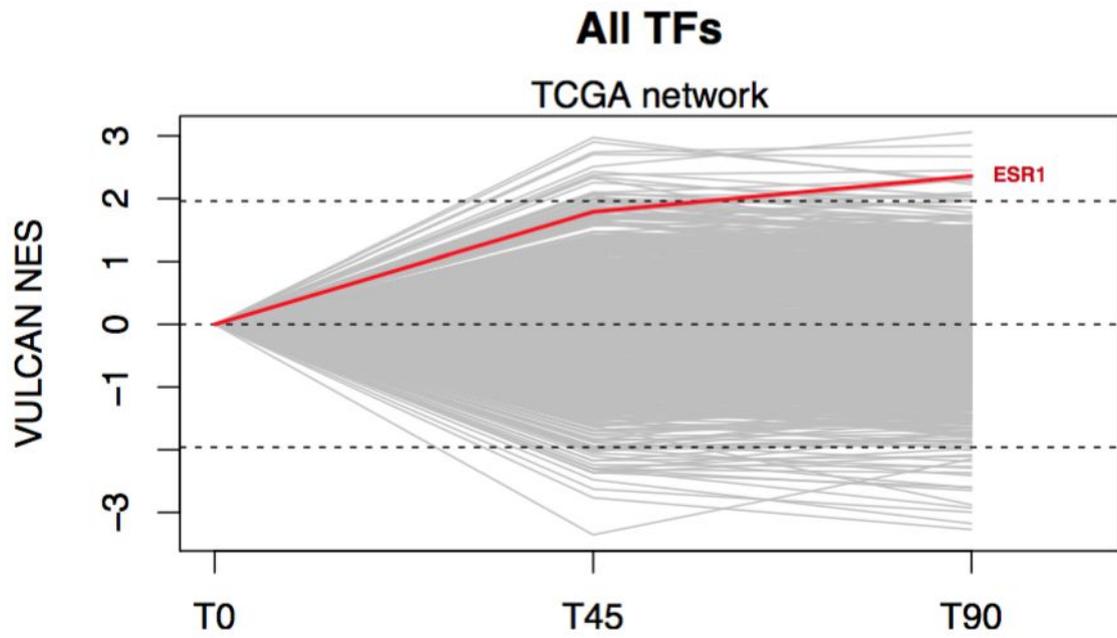


Fig. S15: Global TF activity after Estradiol Treatment in MCF7 cells, inferred using the TCGA network, highlighting the ESR1 TF as an example.

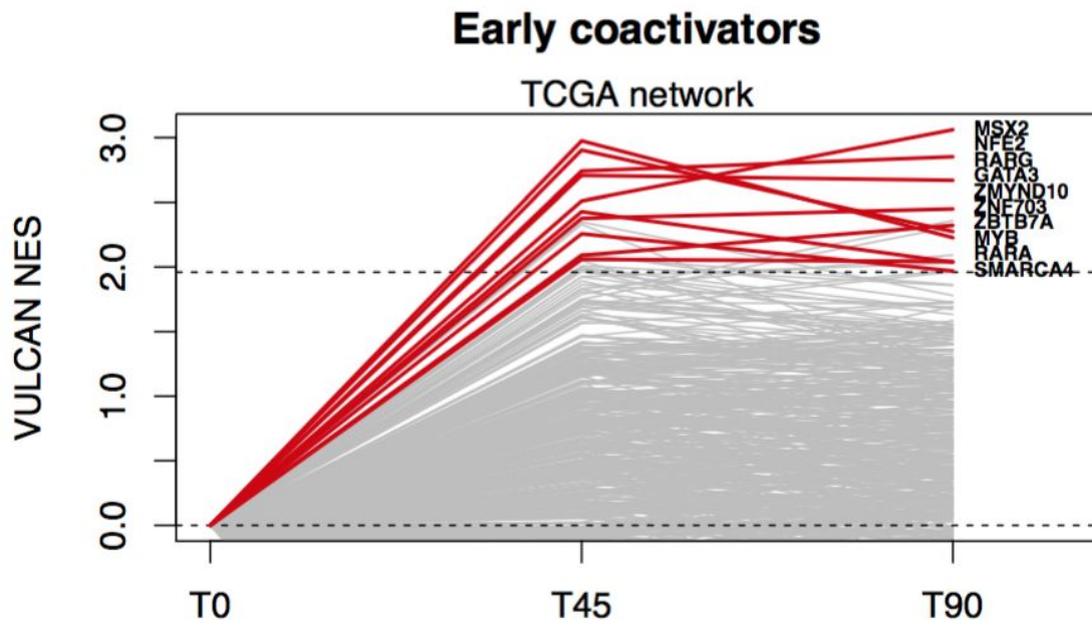


Fig. S16: Global TF activity after Estradiol Treatment in MCF7 cells, inferred using the TCGA network, highlighting TFs significantly upregulated at 45 minutes and 90 minutes.

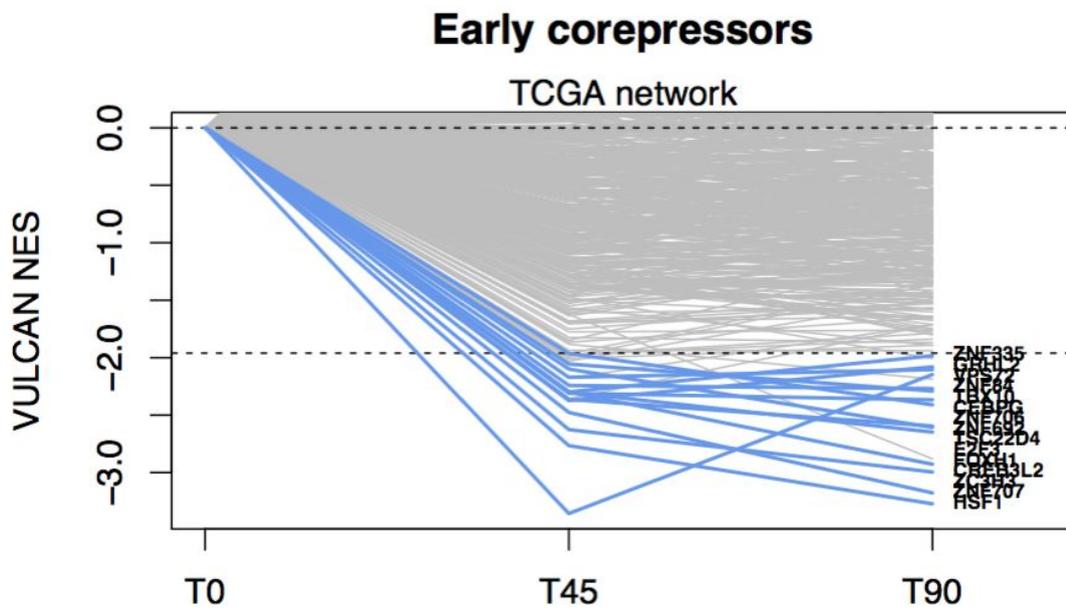


Fig. S17: Global TF activity after Estradiol Treatment in MCF7 cells, inferred using the TCGA network, highlighting TFs significantly downregulated at 45 minutes and 90 minutes.

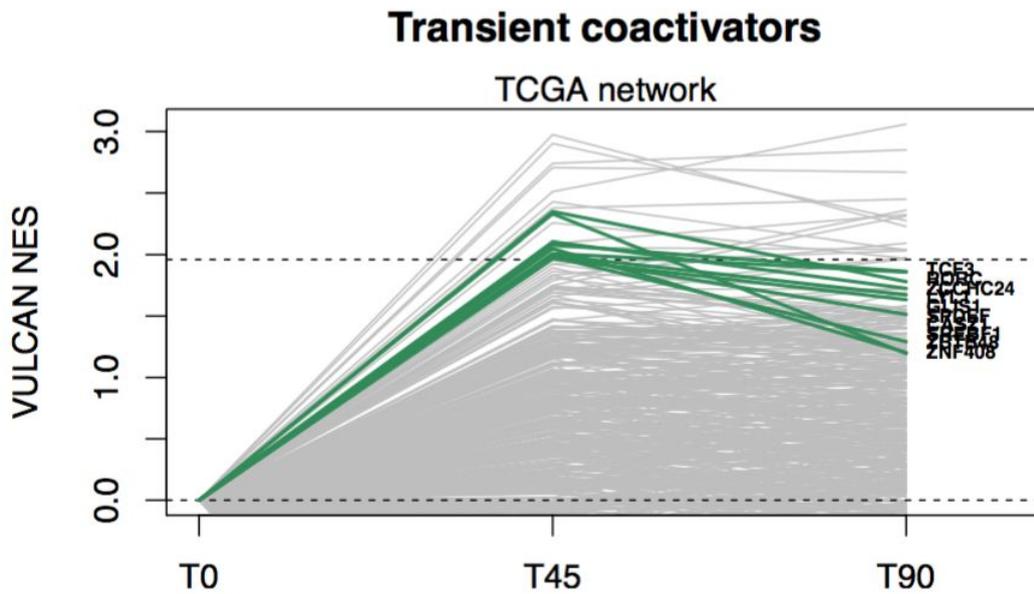


Fig. S18: Global TF activity after Estradiol Treatment in MCF7 cells, inferred using the TCGA network, highlighting TFs significantly upregulated at 45 minutes but not at 90 minutes.

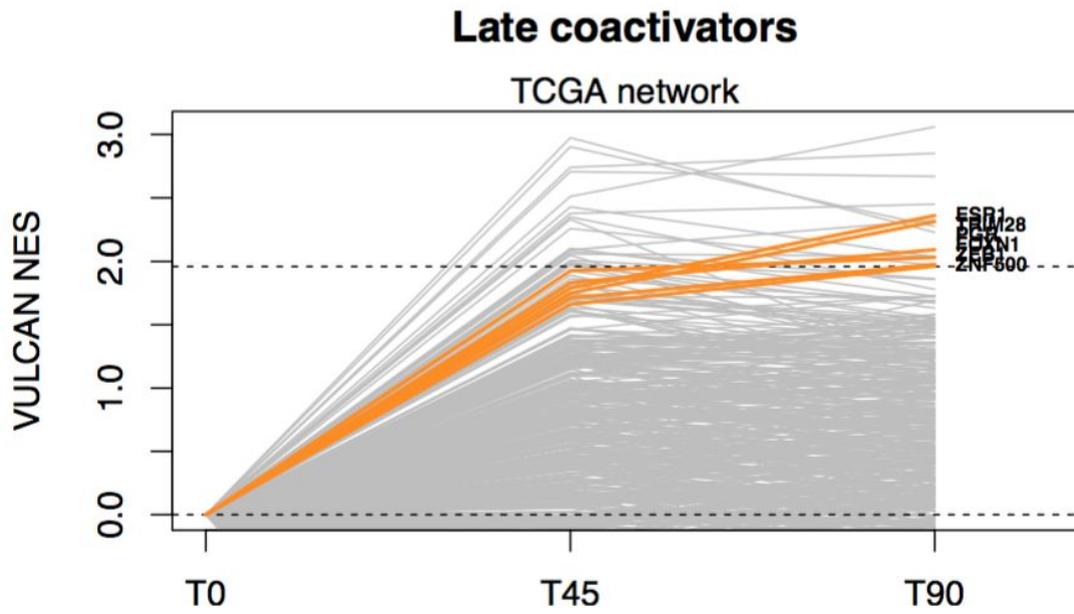


Fig. S19: Global TF activity after Estradiol Treatment in MCF7 cells, inferred using the TCGA network, highlighting TFs significantly upregulated at 90 minutes but not at 45 minutes.

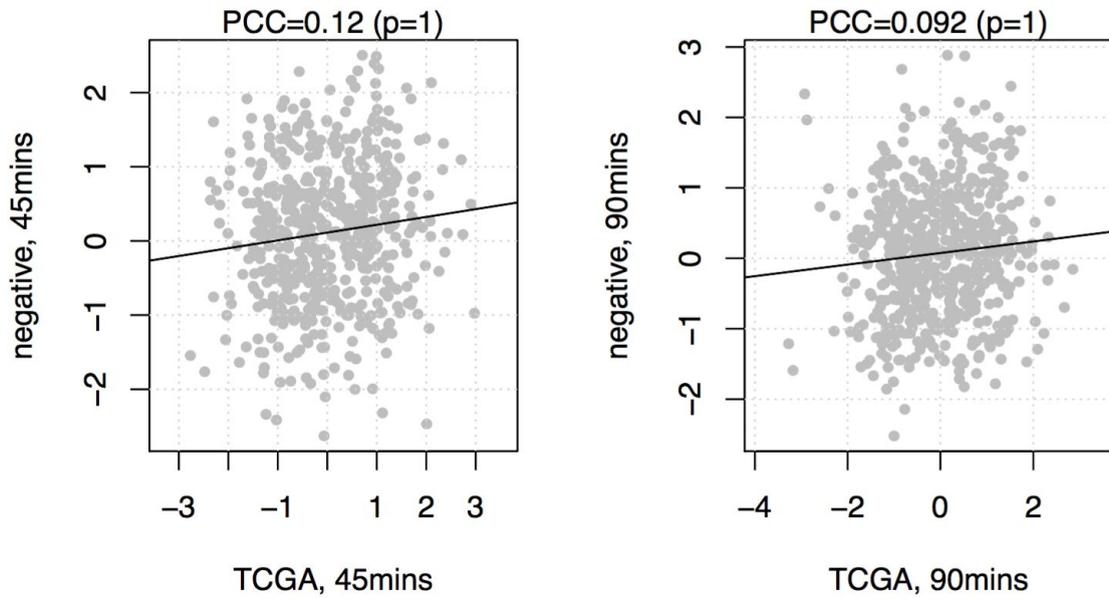


Fig. S20: Comparison between activities inferred through a breast cancer TCGA dataset and the AML dataset. PCC indicates the Pearson Correlation Coefficient.

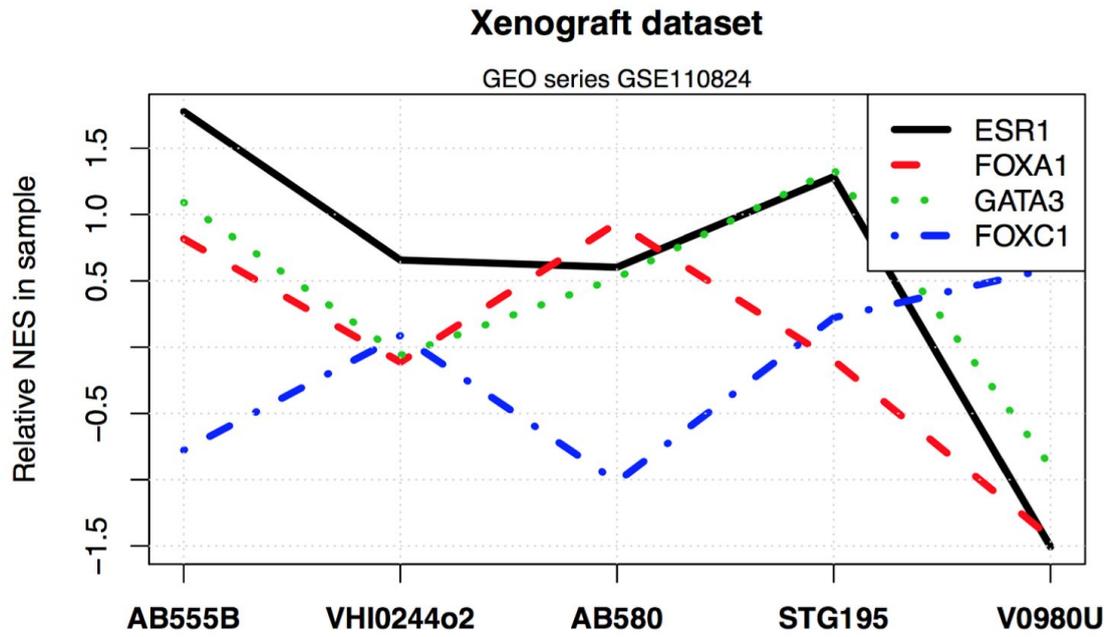


Fig. S21: VULCAN Activity scores for a few TFs extracted from the ER-targeted ChIP-Seq Xenograft (dataset GSE110824).

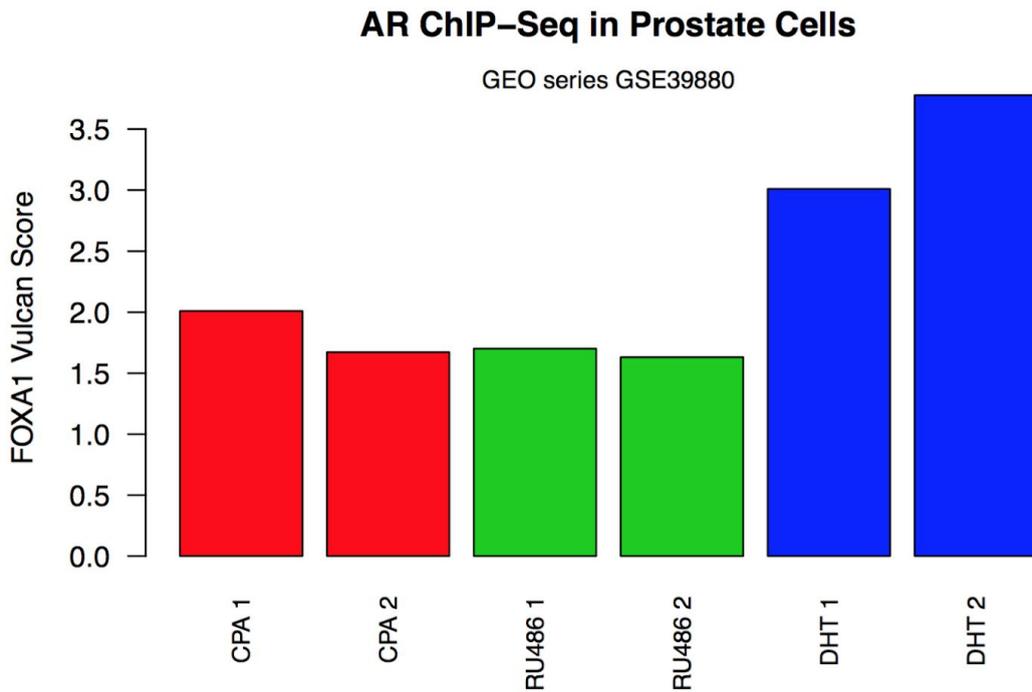


Fig. S22: VULCAN Activity scores for FOXA1 in Prostate cell lines (dataset GSE39880).

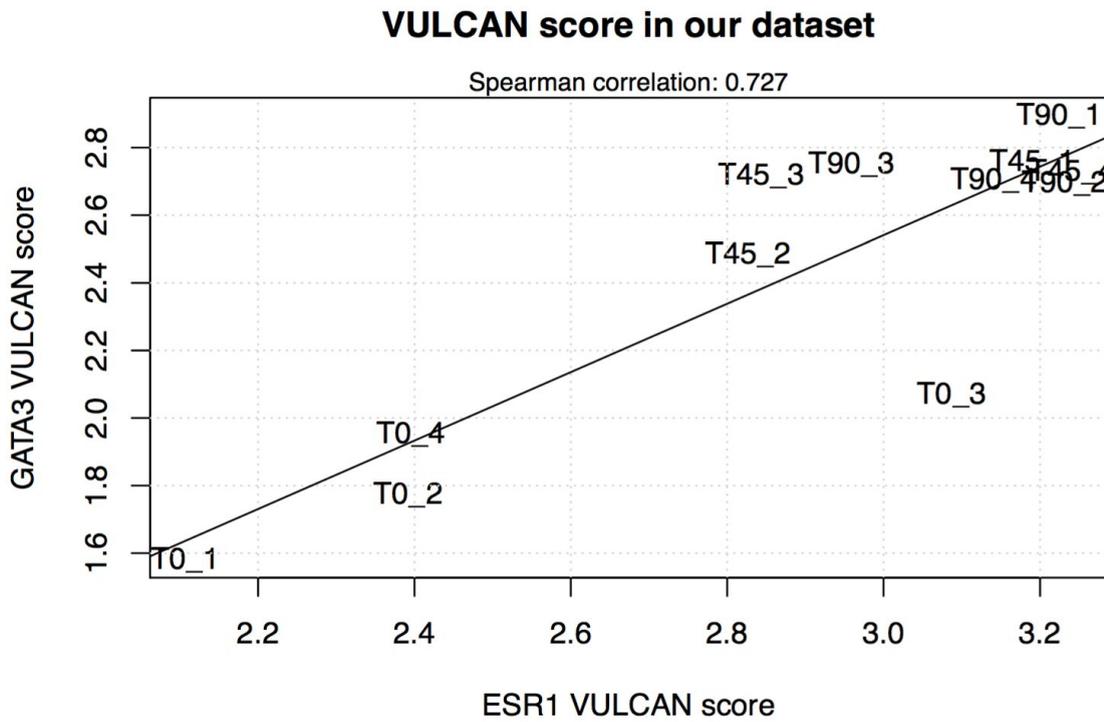


Fig. S23: VULCAN scores of GATA3 and ESR1 in our dataset. Individual samples are indicated.

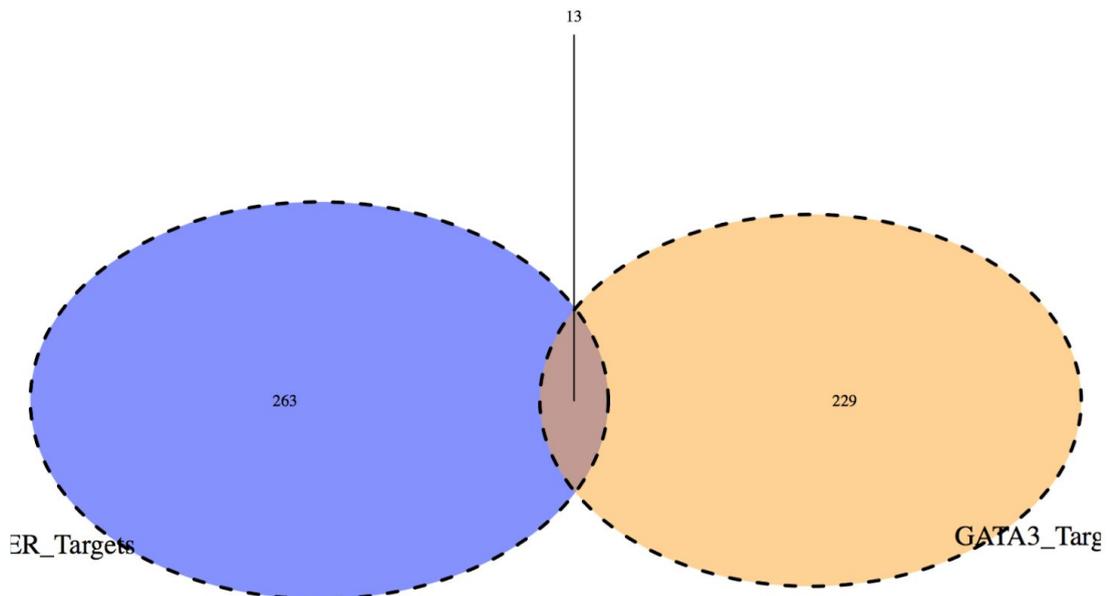


Fig. S24: Example of target intersection between GATA3 and ER according to the MSigDB database of canonical TF-specific motifs in putative target gene promoters.

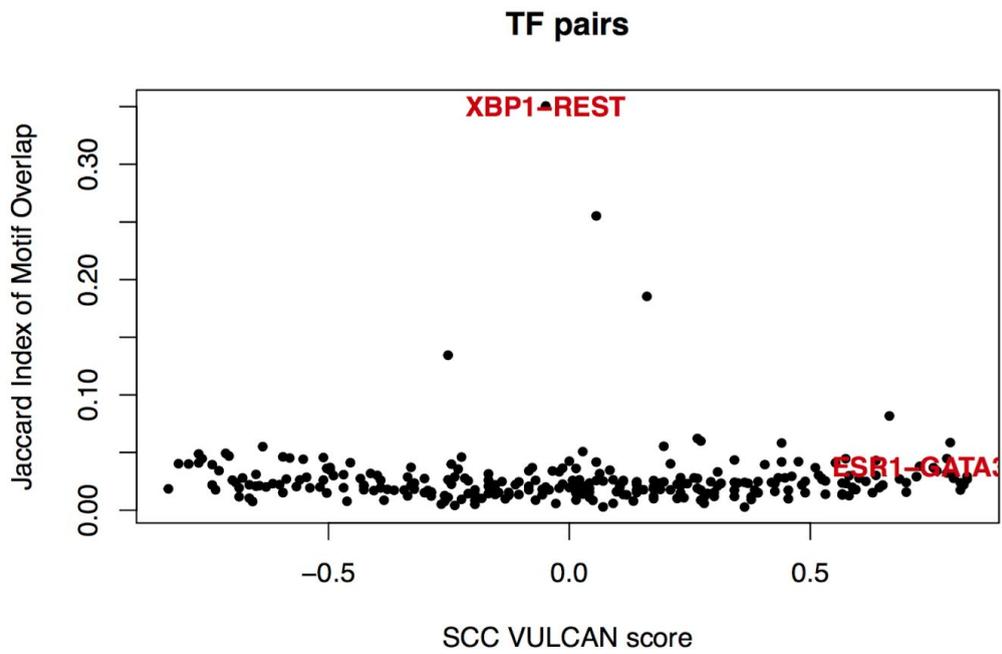
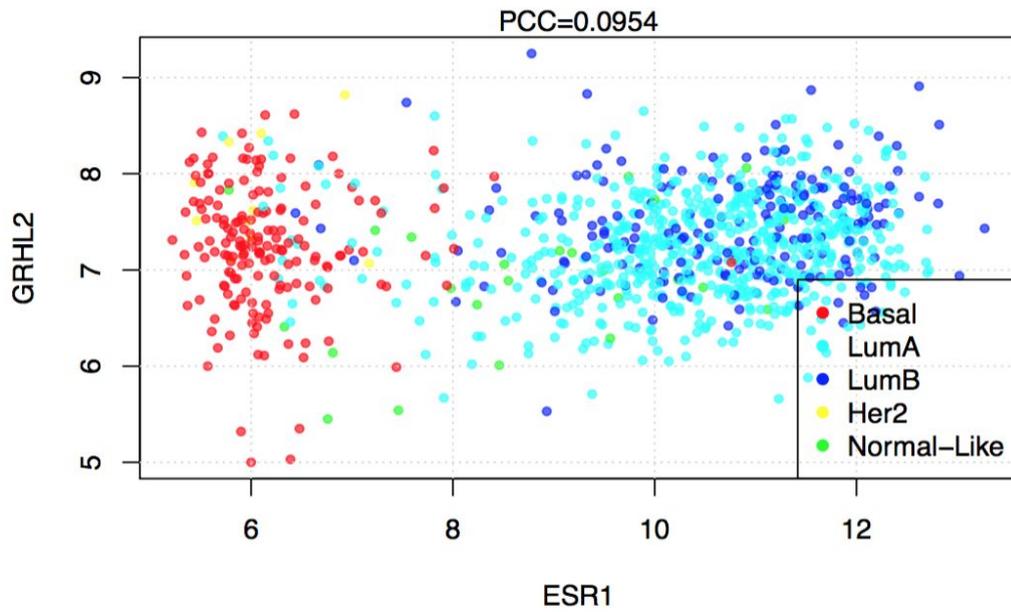


Fig. S25: TF pairs compared in terms of VULCAN score Spearman Correlation Coefficient in our ER dataset and in terms of Jaccard Index of motif-based target intersection according to the MSigDB C3 collection.

Correlation between GRHL2 and ESR1 expression in METABRIC



Correlation between GRHL2 and ESR1 expression in TCGA

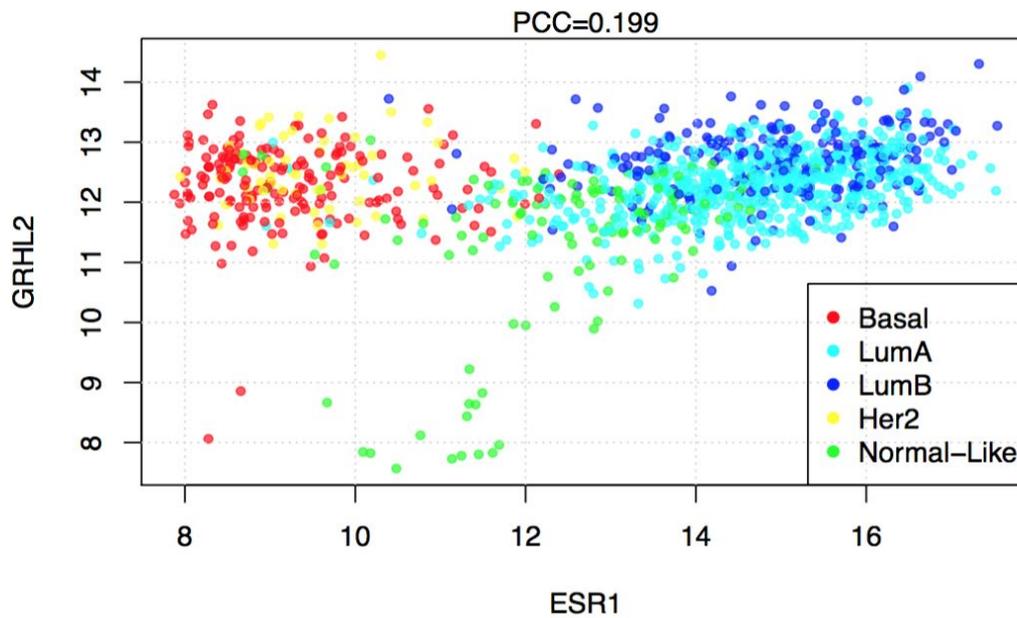


Fig. S26: Correlation between GRHL2 and ESR1 expression in the TCGA & METABRIC breast cancer datasets.

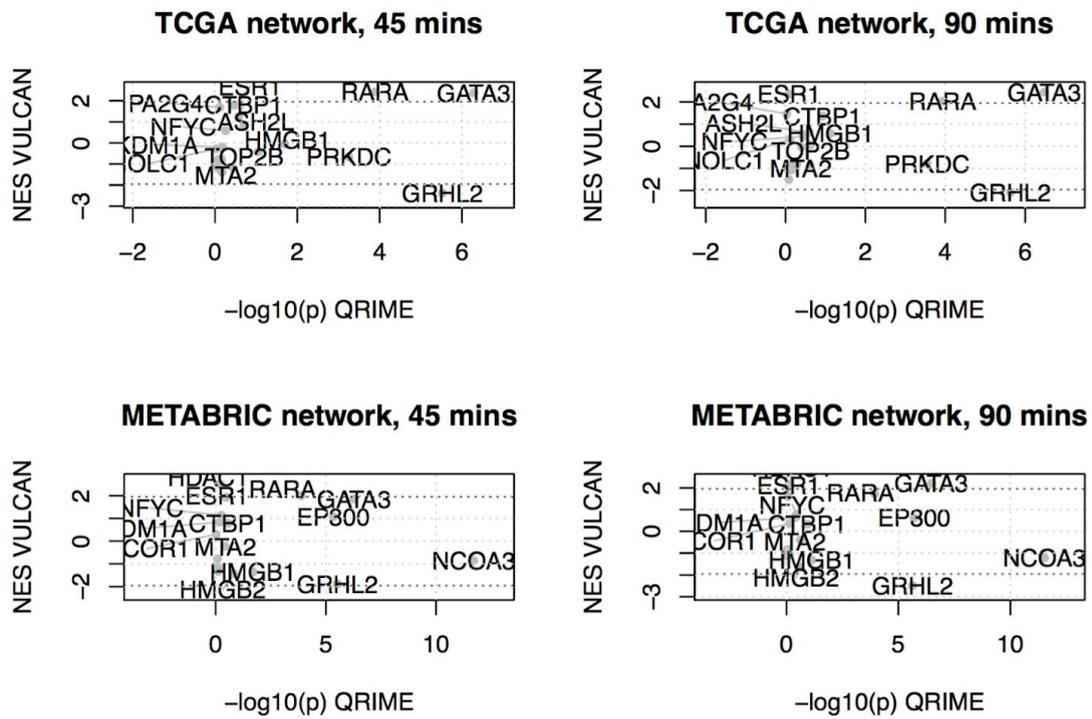


Fig. S27: Comparison of Normalized Enrichment Score between the QRIME method (x-axis) and the VULCAN method (y-axis) at two time points using two regulatory networks for VULCAN

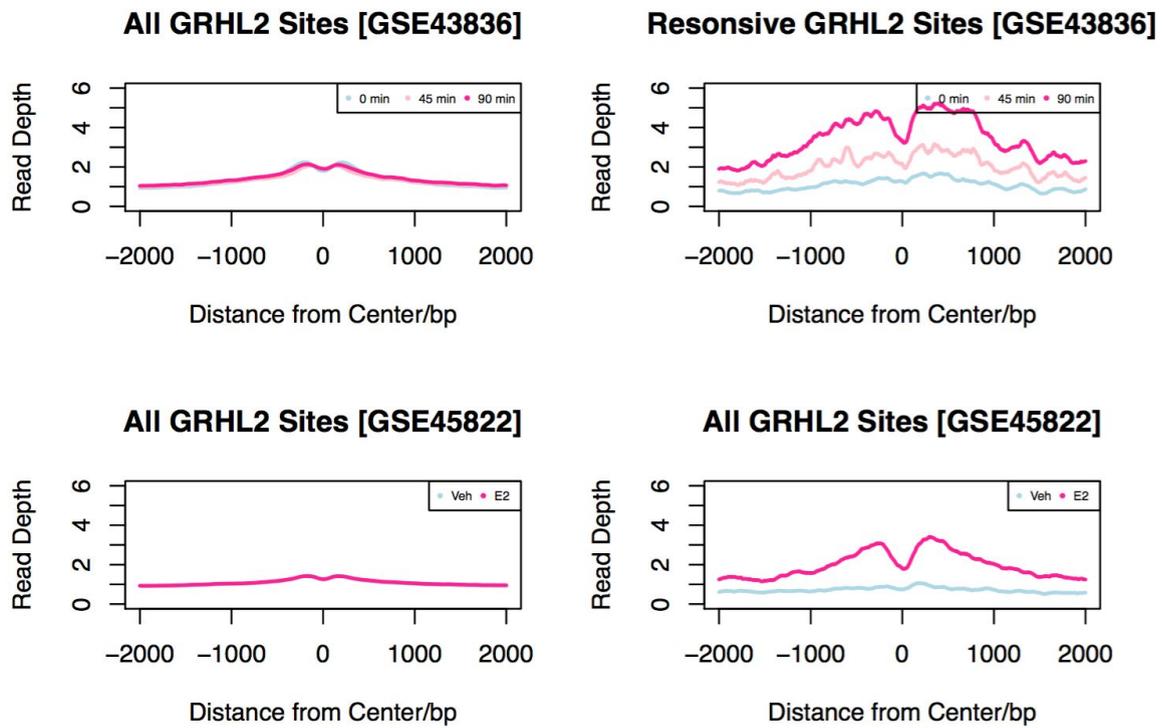


Fig. S28: Analysis of GRHL2 sites of Gro-Seq data from GSE43836 and GSE45822 both showed that E2 responsive GRHL2 responsive sites are transcriptionally responsive to E2.

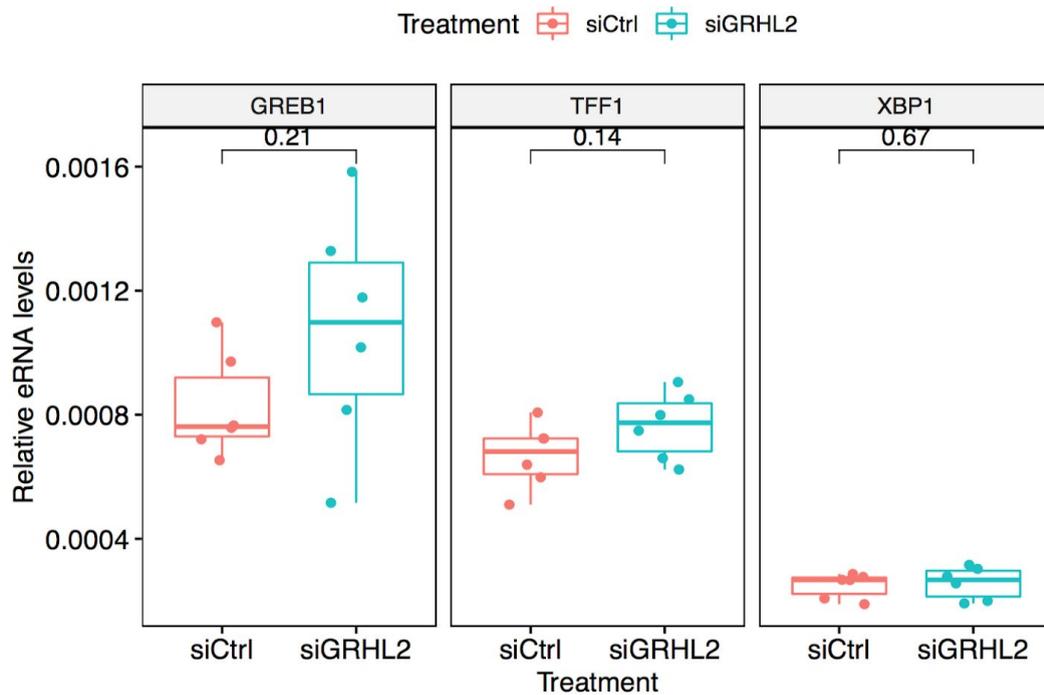


Fig. S29: Effect of knockdown of GRHL2 on eRNA at E2 responsive binding sites.

Supplementary Tables

	NES, 90' vs 0'	pvalue
<i>Bhat esr1 targets not via akt1 up</i>	10.3	4.6e-25
<i>Bhat esr1 targets via akt1 up</i>	10.3	5.3e-25
<i>Dutertre estradiol response 6hr up</i>	8.87	7.1e-19
<i>Frasor response to estradiol up</i>	4.93	8.3e-07
<i>Dutertre estradiol response 24hr up</i>	4.9	9.7e-07
<i>Stein esr1 targets</i>	4.04	5.3e-05
<i>Stein esrra targets responsive to estrogen dn</i>	3.74	0.00018
<i>Creighton endocrine therapy resistance 1</i>	3.72	2e-04
<i>Stossi response to estradiol</i>	3.67	0.00024
<i>Zwang egf interval dn</i>	3.55	0.00039
<i>Creighton endocrine therapy resistance 4</i>	3.42	0.00062
<i>Pedrioli mir31 targets up</i>	3.38	0.00071
<i>Massarweh tamoxifen resistance dn</i>	3.24	0.0012
<i>Lein pons markers</i>	3.19	0.0014
<i>Reactome hs gag degradation</i>	3.19	0.0014
<i>Jiang tip30 targets dn</i>	3.17	0.0015
<i>Kegg glycerophospholipid metabolism</i>	3.16	0.0016
<i>Geserick tert targets dn</i>	3.13	0.0018
<i>Gross hypoxia via hif1a dn</i>	3.09	0.002
<i>Valk aml cluster 6</i>	3.09	0.002

Table S1: aREA results: upregulated MsigDB pathways at 90mins.

	NES, 45' vs 0'	pvalue
<i>Bhat esr1 targets via akt1 up</i>	10.8	3e-27
<i>Bhat esr1 targets not via akt1 up</i>	10.4	2.8e-25
<i>Dutertre estradiol response 6hr up</i>	8.1	5.5e-16
<i>Frasor response to estradiol up</i>	4.54	5.6e-06
<i>Stein esrra targets responsive to estrogen dn</i>	4.21	2.6e-05
<i>Dutertre estradiol response 24hr up</i>	4.15	3.4e-05
<i>Stein esr1 targets</i>	4.03	5.6e-05
<i>Vantveer breast cancer esr1 up</i>	3.84	0.00012
<i>Geserick tert targets dn</i>	3.69	0.00022
<i>Pedrioli mir31 targets up</i>	3.61	3e-04
<i>Reactome glycerophospholipid biosynthesis</i>	3.39	0.00069
<i>Zwang egf interval dn</i>	3.38	0.00072
<i>Naba ecm affiliated</i>	3.31	0.00093
<i>Stossi response to estradiol</i>	3.29	0.00099
<i>Lien breast carcinoma metaplastic vs ductal dn</i>	3.25	0.0011
<i>Kegg glycerophospholipid metabolism</i>	3.25	0.0012
<i>Creighton endocrine therapy resistance 1</i>	3.24	0.0012
<i>Reactome hs gag degradation</i>	3.21	0.0013
<i>Valk aml cluster 6</i>	3.2	0.0014
<i>Massarweh tamoxifen resistance dn</i>	3.1	0.0019

Table S2: aREA results: upregulated MsigDBpathways at 45mins.